# Retention Patterns of Antimony in Mice Following Inhalation of Particles Formed at Different Temperatures[1] (37632)

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There are many radioisotopes of antimony generated in the nuclear fission process. These have various yields, energies of emission and half-life, and therefore represent various degrees of potential inhalation hazard in the case of an accidental airborne release. In such an incident the physical and chemical properties of the released antimony aerosol may also vary considerably depending upon the prevailing conditions. One of the factors which may play an important role in determining these properties is that of temperature of generation of the radioactive particles.

To date, only limited experimental studies have been performed with antimony, most of these having been with an organic base for medical purposes. Djuric, Thomas and Lie (1) have done the most comprehensive inhalation studies using aerosols of the trichloride in rats. They found a significant concentration in the red blood cells, with additional long-term retention in liver, lung and spleen. They reported little or no localization in the bone but an effective whole-body retention of approximately 44 days. Various investigators have indicated a difference in antimony metabolism depending upon the valence state, with most emphasis being placed on the greater affinity for the trivalent form to localize in red blood cells (2–4). These studies have all dealt with parenteral types of administration and not the inhalation route.

The data to be presented are from a study in which mice were exposed to aerosols containing $^{124}Sb$, which were generated at various temperatures. This isotope was used because of its convenient nuclear properties (60 day half-life; $>$ 0.6 MeV $\gamma$-emissions), recognizing that information could be extrapolated from $^{124}Sb$ to other antimony isotopes representing different degrees of potential hazard. Whole-body retention patterns were determined with time, and periodic serial sacrifice yielded tissue distribution data. This report indicates the differential retention observed with those aerosols generated at various temperatures, the highest temperatures showing the least degree of solubility.

*Materials and Methods.* Three groups of 48 mice each were exposed by inhalation to aerosols containing $^{124}Sb$, in a system that yielded "head-only" exposures. The mice were 35 day old females of the Charles River CD-1 strain (Charles River Breeding Laboratory, Wilmington, MA). The exposure apparatus can accommodate 60 mice/exposure run. The mice were placed into test tubes from which the bottom had been partially cut away and they were held in position by pushing a rubber stopper against their hind quarters. The tubes protrude into the aerosol stream through tight-fitting holes in the sides of the apparatus, such that the animal's nose and head are exposed. Each exposure run is of about 10-min duration. Immediately following exposure and at intervals thereafter, the animals were whole-body counted in a large liquid scintillation well detector. The mice were housed in wire-meshed bottom cages, four to a cage and were given water and food *ad libitum* (Wayne Mouse Breeder Blox, Allied Mills, Inc., Chicago, IL.) Serial sacrifices for tissue distribution (four per point) were made at 0, 2, 4, 8, 16 and 32 days postexposure. The remaining animals

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[2] Students in the Biology Department of the University of New Mexico on Associated Western Universities fellowship during a major portion of this study.

TABLE I. Physical and Chemical Properties of the $^{124}Sb$ Utilized for Inhalation Exposure of Mice.

| Group | Starting solution concn | | Temp of aerosol formation (°) | Particle size (AMAD)[a] ($\mu$m) | $\sigma_g$[b] |
|---|---|---|---|---|---|
| | $^{124}Sb$ (mCi/ml) | Tartrate (mg/ml) | | | |
| A | 6.5 | 10 | 100 | 1.6 | 1.9 |
| B | 6.5 | 12 | 500 | 0.7 | 1.8 |
| C | 6.5 | 12 | 1100 | 0.3 | 1.3 |

[a] Activity median aerodynamic diameter.
[b] Geometric standard deviation.

in each group were maintained for backup in case of natural death and for continued whole-body counting to 52 days, at which time the radioactivity was approaching background. Gross counting data were obtained on all tissues using NaI (Tl) detectors.

The aerosols were produced from a starting solution of Sb-tartrate complex in 0.1 *M* tartaric acid solution. Droplets were generated using a Lovelace nebulizer (5) and these were passed through a heating column maintained at a different temperature for each group: 100, 500 and 1100°. This gradation of temperatures was expected to produce the soluble Sb-tartrate complex at the lowest temperature, with more insoluble forms being generated at the two higher temperatures. More details concerning the method of aerosol production may be found elsewhere (6). The size distribution of the aerosols was determined using a Cascade impactor (7). The characteristics of the particular aerosols used in this study are summarized in Table I.

*Results.* The serial whole-body counts yielded a retention pattern (Fig. 1) generally similar to that observed in small animals following inhalation of a moderately insoluble or insoluble aerosol. It was characterized by an early period of rapid clearance followed

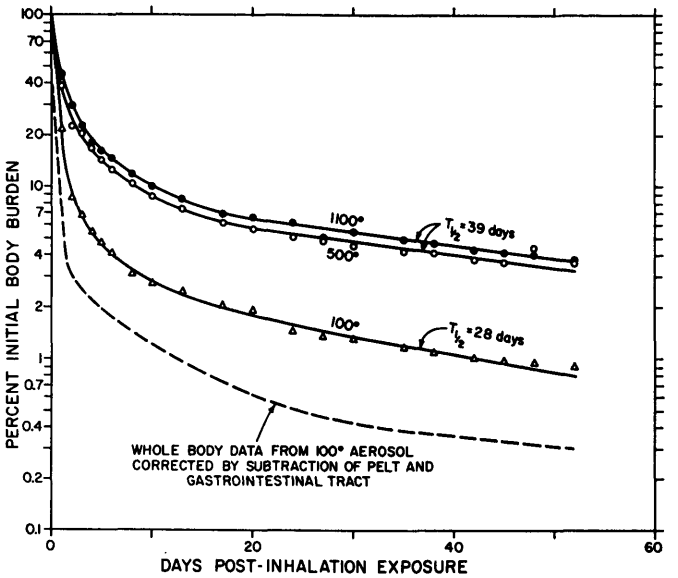


FIG. 1. Whole-body retention of $^{124}Sb$ as a function of the temperature of aerosol production from an initial solution of the tartrate. (- -) The adjusted whole-body curve for one temperature aerosol, when the pelt and gastrointestinal $^{124}Sb$ were subtracted from the whole-body activity.

TABLE II. Percentage of Total Body $^{124}Sb$ in Pelt and Gastrointestinal Tract.

| Time (days) | Pelt | | Gastrointestinal tract | Total |
|---|---|---|---|---|
| | Head | Body | | |
| | | 100° | | |
| 0 | 21 | 4 | 53 | 78 |
| 1 | 24 | 7 | 29 | 59 |
| 2 | 36 | 6 | 22 | 65 |
| 4 | 40 | 11 | 8 | 59 |
| 8 | 31 | 16 | 9 | 55 |
| 16 | 38 | 18 | 8 | 64 |
| 32 | 36 | 28 | 3 | 66 |
| 52 | 34 | 25 | 4 | 62 |
| | | 500° | | |
| 0 | 13 | 6 | 42 | 61 |
| 1 | 28 | 7 | 23 | 58 |
| 2 | 26 | 6 | 11 | 44 |
| 4 | 20 | 9 | 10 | 38 |
| 8 | 39 | 15 | 5 | 59 |
| 16 | 43 | 16 | 7 | 66 |
| 32 | 39 | 23 | 2 | 64 |
| 52 | 54 | 24 | 1 | 79 |
| | | 1100° | | |
| 0 | 13 | 5 | 27 | 45 |
| 1 | 20 | 7 | 16 | 43 |
| 2 | 15 | 7 | 12 | 34 |
| 4 | 24 | 10 | 7 | 41 |
| 8 | 29 | 14 | 4 | 47 |
| 16 | 37 | 15 | 3 | 55 |
| 32 | 53 | 23 | 2 | 78 |
| 52 | 49 | 23 | 3 | 75 |

by a steady decrease in the rate of loss of radioantimony. The retention patterns for the 500 and 1100° aerosols were nearly similar, while the 100° aerosol was cleared to a greater extent, particularly at early times.

Examination of the tissue distribution data aroused concern as to the meaning of the gross whole-body retention pattern; specifically, the presence of large quantities of radioantimony was not expected in the pelt samples. Although contamination of the head pelt is expected following "head-only" exposures, especially at early time periods postinhalation exposure, the extent to which it persisted and was reflected in the remaining pelt was surprising. The gastrointestinal tract also contained rather large amounts of activity, presumably due to licking and swallowing of $^{124}Sb$. Data on these tissues are presented in Table II as a percentage of the total body $^{124}Sb$ at sacrifice. The sum total percentage of the pelt and gastrointestinal tract is also presented. A plot of this latter for the 100° aerosol is also shown in Fig. 1 to indicate the large contribution that these fractions have on the total body content. A statistical analysis of the data in Table II indicated that no difference in total $^{124}Sb$ activity existed between aerosol temperatures, at the $F(0.95)$ level. Because of this large contribution to the body burden from the contaminated pelt and the gastrointestinal tract content from licking, tissue data presented in the remainder of this report will be expressed in terms of the corrected or adjusted body burden.

Data from lung tissue, expressed as a percentage of the adjusted whole-body burden, are shown in Fig. 2. There is an approximate order of magnitude difference between the 100° aerosol and those at 500 and 1100°. This difference is reflected in Fig. 3 in which the femur data are shown on a similar ordinate. The more soluble material at 100° leaves the lung and deposits primarily in skeleton. This is magnified in Fig. 4 which shows the significant differences in absolute amounts residing in carcass, a reflection of skeletal deposition. The data from liver analyses (Fig. 5) do not reflect the pattern observed for skeleton. (Although the 100° material entered blood to a far greater extent, there was a differential uptake of the higher temperature material by liver.) This presumably is related to the chemical (and/or physical) form of the blood-borne material or, perhaps, the rate of entry into the blood stream. The extent of absorption from the gastrointestinal tract should not be overlooked in this, although recent data would indicate a maximum absorption of 1–2% following gavage (8).

Whole blood samples at 2 days postexposure gave values of 0.43% of the adjusted body burden/cc for the 100° aerosol, 1.2%/cc at 500° and 1.0%/cc at 1100°. All values were essentially the same (0.37%/cc, 1.2%/cc, 0.93%/cc) at 4 days postexposure.

*Discussion.* The aerosol data in Table I show a marked change with temperature. At 100° the particles may be considered chemi-

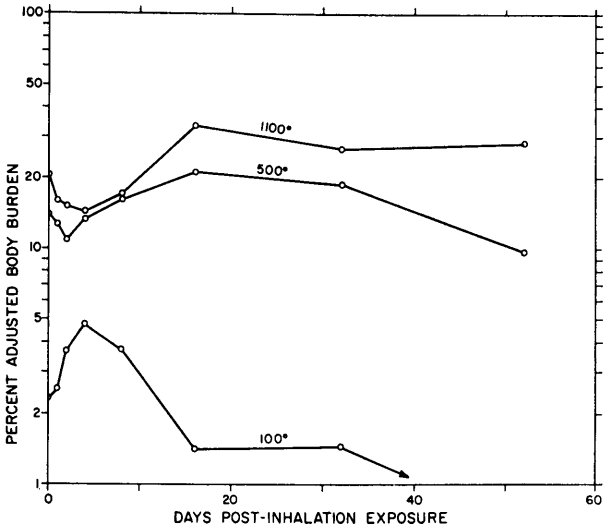


FIG. 2. $^{124}$Sb activity in the lung as a percentage of the adjusted whole-body burden at time of sacrifice.

cally the same as the starting complex, antimony tartrate. As the temperature increased the organic portion was degraded, thus reducing the particle size. At 1100° the antimony particles were probably in the form of condensation nuclei, having an even smaller aerodynamic diameter and a geometric standard deviation of only 1.3. This latter parameter would indicate a very uniform particle size distribution, probably a result of the condensation process.

The tissue distribution results indicate a marked alteration in $^{124}$Sb retention, depending upon the temperature of generation from the chelate complex. Those particles formed at lower temperatures are more soluble, leaving the lung very soon after deposition and transporting in large degree to bone. The aerosol particles generated at the two highest temperatures tend to remain much longer in lung, with less absolute accumulation in the skeleton. A gradual buildup in skeleton is in-

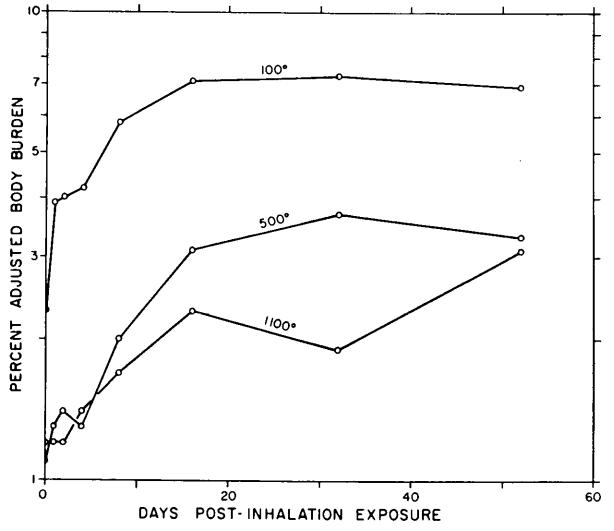


FIG. 3. $^{124}$Sb activity in the femur as a percentage of the adjusted whole-body burden at time of sacrifice.

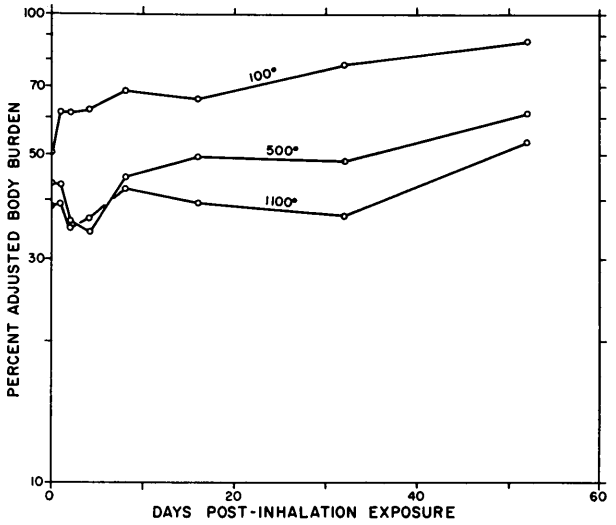


FIG. 4. $^{124}$Sb activity in the carcass (presumed to be a reflection of skeletal content) as a percentage of the adjusted whole-body burden at time of sacrifice.

dicated at all temperatures studied (Figs. 3, 4). Whole-body retention curves show a somewhat similar pattern of decrease (Fig. 1) and appear to vary only by the amount excreted early via the gastrointestinal tract. This difference in initial excretion may well be a function of particle size, as indicated in Table I. The larger particles at 100° would be expected to deposit in the upper respiratory tract to a relatively larger degree, thus leading to a relatively greater clearance to the gastrointestinal tract. The difference in retention half-life indicated (39 days at the higher temperature vs 29 days at 100°) is doubtless a function of the differences noted in tissue distribution. The indication is that retention of $^{124}$Sb in the lung in the degraded form (500° and 1100°) is no longer than the more soluble form localized in the skeleton.

An indication of the importance of the differences in tissue distribution of $^{124}$Sb may

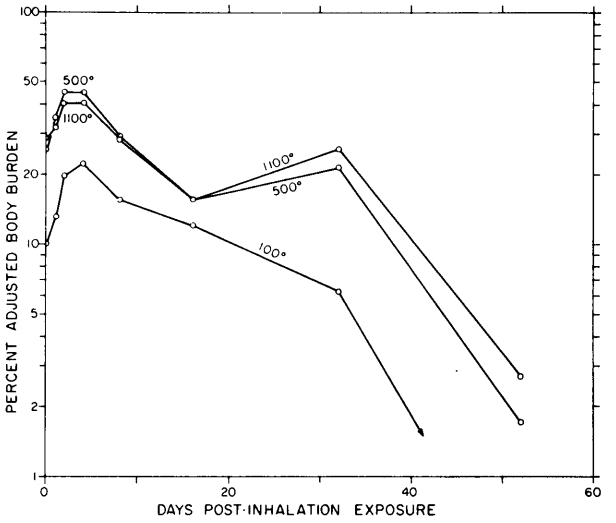


FIG. 5. $^{124}$Sb activity in the liver as a percentage of the adjusted whole-body burden at time of sacrifice.

TABLE III. Estimated Radiation Dose to Femur and Lung Over the 52 Days of the Study for an Assumed Initial Adjusted Body Burden of 1 $\mu$Ci $^{124}$Sb.

| Temp (°) | Dose (rads)[a] | | |
|---|---|---|---|
| | Lung | Femur | Lung ÷ femur |
| 100 | 9 | 26 | 0.3 |
| 500 | 55 | 9 | 6.1 |
| 1100 | 76 | 8 | 9.5 |

[a] An average beta energy of 0.35 MeV/disintegration was assumed.

be seen in Table III. This gives estimated radiation doses to lung and femur for an assumed initial body burden of 1 $\mu$Ci. First, note the gradation within each organ as the temperature of aerosol production was increased. There is an 8.6-fold increase in dose to the lung and a 3.3-fold decrease in the dose to the femur. Second, as indicated in the last column of Table III, the femur would receive $\sim$ 3 times the dose to lung with the lower temperature aerosol, but the lung with the 1100° aerosol would receive $\sim$ 10 times the dose to the femur. These two points serve to stress the important influence that temperature of aerosol release would have on the choice of the organ expected to receive the greatest radiation insult.

The pelt sample activity observed in this study perhaps needs further investigation. The similar pattern in retention throughout the experiment, in both head and remaining pelt suggests a contamination problem. Djuric, Thomas and Lie (1) did find some localization in pelt, but this was consistently only 3–4% of the body burden through 140 days postexposure. Their studies were apparently "clean" with little or no external contamination allowed. This amount is several times lower than in the present studies. The amount of $^{124}$Sb in either pelt sample is essentially the same with all temperature aerosols also indicating primarily a contamination phenomenon. It is difficult from the data at hand to determine how much pelt activity is from the metabolism of $^{124}$Sb and how much is residual contamination.

According to the International Commission on Radiological Protection (ICRP) the amount of antimony in skeleton is 25% of that in the total body and has an effective half-life of 38 days for $^{124}$Sb (9). Our data would indicate a much larger deposit in the skeleton with the lower temperature aerosols (approx 85% of the body burden at 52 days) but according to the whole-body data (Fig. 1) the half-life of retention may be somewhat similar. The high temperature aerosols, obviously the more insoluble forms, present a very interesting pattern of radiation dose distribution. The lung appears to be the critical organ for receiving the largest dose, but there is still a significant translocation to the skeleton and liver. It is possible that with continued exposures the concentration in bone could surpass that in lung, making the former the critical organ, regardless of chemical form. This might particularly be the case if a factor for uneven distribution in bone were employed. The Task Group on Lung Dynamics (10) suggests that antimony compounds have retention times of the order of weeks. The data presented here on mice would enforce this premise, regardless of whether the target organ were lung or skeleton. Longer term studies are needed to more precisely determine this.

*Summary.* The temperature of aerosol formation has been demonstrated to profoundly influence the metabolic pattern of inhaled antimony. Using $^{124}$Sb as a tracer, aerosols were nebulized from the tartrate complex and the droplets passed through heating columns at 100, 500 and 1100°, before reaching the animal. The lower temperature aerosol was more soluble and left the lung rapidly, localizing primarily in skeleton. The two higher temperature-produced aerosols resulted in $^{124}$Sb remaining in the lung for extended periods. Overall retention, regardless of the critical organ (lung or skeleton), would tend to place antimony in the class of compounds that have a retention time on the order of weeks.

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